

REMARKS

Undersigned counsel thanks Examiner Nguyen for extending the courtesy of a telephone interview held on February 22, 2005 to discuss the outstanding Office Action and the contents of this Response.

Status of the claims

Claims 1-40 were pending in this application. Claims 1-9, 11-21, 23-36, and 38-40 were under active consideration following withdrawal of claims 10, 22, and 37 as non-elected species. Claims 1, 8, 15, 16, 21, 23 and 25 have been amended; claims 2, 11, 35, 36, and 38 have been canceled without prejudice. Upon entry of these amendments, claims 1, 3, 4, 6-10, 12-34, 37, 39, and 40 will be pending with claims 1, 3, 4, 6-9, 12-21, 23-34, 39 and 40 under active consideration. Claims 1, 16, and 21-23 are independent.

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present invention. Reconsideration and withdrawal of the rejections set forth in the above-identified Office Action are respectfully requested.

Claim amendments

Claims 1, 16, 21 and 23 have been amended to now recite that the donor "liver" tissues are obtained "greater than about 2 hours postmortem." The amendments find support throughout the specification and claims as filed, particularly in paragraphs 186 and 14 and in original claim 33-35.

Applicants submit respectfully that the amendments presented herein are supported fully by the claims and/or specification as originally filed and, thus, do not represent new subject matter.

Claim objections

Claims 8, 15, and 25 are objected to for allegedly containing non-elected embodiments or species. Claim 8 and 25 have been amended to solely recite the species "adult," and claim 15 has been amended to solely recite the species "hepatic cell lineage" in accordance with

Applicants' Election dated January 16, 2003. The amendments have been entered without disclaimer of or prejudice to pursuing the non-elected subject matter in this or other applications, for prosecution on the merits, and to which the claims shall be restricted if no generic claim is finally held to be allowable.

Accordingly, Applicants respectfully submit that the claim objections have been overcome.

Claim rejections under 35 U.S.C. §112, second paragraph

Claims 1-9, 11-21, 23-26 and 38-40 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out particularly and claim distinctly the subject matter regarded as the invention for the reasons of record. In sum, the Office Action alleges that "since the criteria or conditions that are used for considering a non-fetal donor tissue to be unsuitable or suitable for organ transplantation are not explicitly defined in the specification and are inherently subjective, the metes and bounds of the claims are not clearly determined." Applicants traverse respectfully.

Without acquiescing in the propriety of rejection, and solely to advance prosecution of the present application, claims 1, 16, 21 and 23 have been amended to recite that the donor tissues are obtained "greater than about 2 hours *postmortem*." (emphasis added).

On this basis, Applicants suggest respectfully that the rejections have been overcome, and Applicants request respectfully that the 35 U.S.C. § 112, second paragraph, rejections be withdrawn.

Claim rejections under 35 U.S.C. § 102

Claims 1-9, 11-17, 19-20 and 39-40 stand rejected as allegedly being anticipated by PCT Application No. WO 95/13697 to Reid *et al.* (hereinafter, "Reid"), under 35 U.S.C. § 102(b). The Office Action alleges that none of the claims recite that the organ tissue has been exposed to a period of ischemia, in particular warm ischemia, for a time period that the organ has suffered irreversible damage and has become unsuitable for organ transplantation. Further, it is alleged that since the criteria for a tissue to be considered unsuitable for an organ transplantation are not

explicitly defined, the method of Reid would be considered to be unsuitable. Applicants traverse respectfully on the following grounds.

First, Applicants respectfully submit that the criteria for a tissue to be considered unsuitable for an organ transplantation is now abundantly clear in the claims, as amended. Claims 1 and 16, 21 and 23 recite a method of processing non-fetal donor tissue obtained *greater than about 2 hours* postmortem. In contrast, as the Office Action acknowledges, Reid does not teach specifically that the donor has a non-beating heart at the time when the tissue is harvested. Rather, as the Examiner notes, the livers of Reid are harvested *immediately* upon death (page 14, lines 9-15). Thus, Applicants submit respectfully that Reid does not teach or suggest a method of obtaining progenitor cells from tissue obtained greater than about 2 hours postmortem and does not read on the method taught in Reid.

Second, Applicants respectfully submit that the limitation “obtained greater than about 2 hours postmortem” would be clear to the one of ordinary skill in the art at the time the invention was conceived that such livers have become unsuitable for organ transplantation. As will be discussed in greater detail below, no livers greater than about 2 hours postmortem had ever been transplanted prior to or after the filing date of the instant application and therefore said liver greater than about 2 hours postmortem logically would have considered unsuitable for transplantation. Therefore, the method disclosed in Reid cannot and does not teach each and every element of the claimed method.

In view of the reasons above, Applicants submit respectfully that the claims of the present invention, as amended, are not anticipated by Reid. Accordingly, Applicants request respectfully that the rejection to claims under 35 U.S.C. § 102(b) be withdrawn.

Claims 1-2, 8-9, 11-12, 16-21, 23-26 and 38-40 further stand rejected as allegedly being anticipated by U.S. Patent No. 6,129,911 to Faris (hereinafter, “Faris”), under 35 U.S.C. § 102(e) for the reasons of record. Briefly, the Office Action alleges that Faris discloses methods of isolating progenitor cells from deceased donors or cadavers, neither of which have beating hearts. Applicants traverse respectfully.

Applicants submit respectfully that the independent claims, as amended, are not anticipated by Faris, because Faris does not disclose each and every element of those amended

claims as is required for a *prima facie* showing of anticipation. As noted above for Reid, Faris similarly does not teach or suggest obtaining progenitor cells from donor tissues obtained greater than about 2 hours postmortem. While Faris does disclose at column 5, lines 6-7, that tissue may be obtained from a deceased donor or an aborted fetus, the method for isolating progenitors actually disclosed by Faris, at column 6, lines 5-23, provides that the isolation process begins immediately following *anesthetization* of the donor, *i.e.*, while the donor is still alive with a beating heart. In fact, the art available at the time of Faris taught that an organ may remain suitable for transplant only for a limited time following cessation of the donor's heartbeat.

This conclusion is further supported by data collected by the Scientific Registry of Transplant Recipients ("SRTR"). The table below shows the warm ischemic time (minutes) after cardiac death of liver donors in the United States:

Year	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
N	9	10	8	12	17	24	23	39	70	79	113
Mean	67	60	60	50	51	51	51	41	38	37	35
Minimum	46	30	38	30	1	19	1	1	1	0	1
Maximum	110	84	83	60	95	99	78	87	99	85	126

Thus, for a span of *nine* years, leading up to and including the filing date of the instant application (*i.e.*, 2001), **not a single** liver was transplanted from donors with a warm ischemic time of greater than about 2 hours. In fact, of the 404 liver transplants during the 11 year time span tabulated above, entirely 403 of them were with livers explanted *within* 2 hours of death. Put simply, one skilled in the art, being aware of this data, could only reasonably conclude that tissue greater than about 2 hours postmortem is unsuitable for transplantation.

Accordingly, in view of the teachings of Faris, and in light of the available art at the time which taught that an organ may remain suitable for transplant for only a limited time following death, Applicants submit respectfully that one skilled in the art would *not* be taught by Faris that viable progenitor cells could be obtained from organ tissues that had passed the point of unsuitability (*i.e.*, after about 2 hours postmortem) for transplantation. Hence, Applicants submit respectfully that the claims of the present invention, as amended, are not anticipated by Faris,

and Applicants request respectfully that the rejection of Claims 1-2, 8-9, 11-12, 16-21, 23-26, and 38-40 under 35 U.S.C. § 102(e) be withdrawn.

Claim rejections under 35 U.S.C. § 103(a)

Claims 21, 23-28, 33-36 and 38-40 stand rejected as allegedly being obvious, for the reasons of record, over Reid in view of Faris under 35 U.S.C. § 103(a). In short, the Office Action alleges that Reid teaches methods for isolating liver stem cells from any species. While the Office Action acknowledges that Reid does not teach specifically that the donor has a non-beating heart at the time when the tissue is harvested or that the tissue is harvested within the claimed time windows, the Office Action alleges that Faris cures these deficiencies by teaching the isolation of adult human liver tissue from adult cadavers. Applicants traverse respectfully.

Applicants submit respectfully that there is neither teaching nor suggestion in these references that, as discussed above, viable progenitor cells may be obtained from organ tissue that is unsuitable for transplantation (*i.e.*, obtained greater than about 2 hours postmortem). The Office Action does not allege that Faris cures this deficiency in Reid. In fact, for the reasons expounded above, knowing the data available at that time, Faris could not have considered liver cells obtained greater than about 2 hours even remotely suitable for transplantation.

Thus, without acquiescing in the allegation that Faris may be properly combined with Reid to provide hepatic progenitor cells isolated from adult human cadavers, Applicants submit respectfully that, as Faris fails to cure the deficiencies of Reid with respect to the use of organ tissue unsuitable for transplantation, the combination of the Reid with Faris fails to meet the threshold required for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a).

Accordingly, Applicants submit respectfully that the rejection of Claims 21, 23-28, 33-36, and 38-40 under 35 U.S.C. § 103(a) has been traversed, and Applicants request respectfully that the rejection of Claims 21, 23-28, 33-36, and 38-40 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicants submit respectfully that the present application is in condition for allowance. Favorable reconsideration, withdrawal of the rejections set forth in the above-noted Office Action, and an early Notice of Allowance are requested.

Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 625-3500. All correspondence should be directed to our address given below.

AUTHORIZATION

Applicants believe there is no additional fees due in connection with this filing. However, to the extent required, the Commissioner is hereby authorized to charge any fees due in connection with this filing to Deposit Account 50-1710 or credit any overpayment to same.

Respectfully submitted,



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